DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6009

July 22, 2002

WARNING LETTER

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED

Mr. Anthony H. Wild, Ph.D.
Chairman and CEO
Medpointe Healthcare, Inc.
265 Davidson Avenue, Suite 300
Somerset, New Jersey 08875-6833

File No.: 02-NWJ-26

Dear Dr. Wild:

During May 20 through June 6, 2002, investigators from this office conducted an inspection of your drug manufacturing site, formerly located at Half Acre Road in Cranbury, New Jersey. Our investigators documented significant violations of the current Good Manufacturing Practice (cGMP) Regulations found in Title 21, Code of Federal Regulations (CFR), Parts 210 and 211, with regard to the production of Soma 350 (carispordol) Tablets. These violations cause those products to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

The inspection revealed the following significant deficiencies:

1. Contrary to the requirements of 21 CFR Part 211.192, your firm failed to thoroughly investigate and implement effective corrective actions for the presence of black specks, containing metal particles, which are visibly present on tablet surfaces of Soma 350 Tablets you manufacture.

   Additionally, at the time of the inspection, there was no documented health hazard evaluation to determine the risk associated with the potential metal contamination.

2. The visible inspection system and metal checkers your firm implemented to cull out rejected tablets is inadequate, in that there are no specified limits on the quantity of tablets that can be rejected for visual failures before an investigation is conducted, as required by 21 CFR Part 211.110. For example, rejected tablets were identified for Lots 1G1054, 1H1061 and 1I1083 after an initial pass through a metal checker and visual screening inspection. After a second metal detector screening yielded an even higher number of rejected tablets, there was no follow-up investigation to document the rationale for continued screening.

Additionally, the visual inspection of Soma 350 Tablets examines the outer surface and edges of the tablets. At the time of the inspection, there was no documented inspection or evaluation of the interior of the tablets.

3. Contrary to the requirements of 21 CFR Part 211.65(b), there was no documentation to demonstrate that the [redacted] Metal Detectors were qualified for their intended use and that substances required for operation, such as lubricants, would not alter the quality of the drug products.

4. There is no assurance that the tooling used to compress the Soma 350 Tablets is maintained and acceptable for its intended use, as required by 21 CFR Part 211.67. For example, there was no documented maintenance on the tooling sets used in the production of Soma 350 Tablets since 1995. Also, there was no assessment of the possibility that tools taken out of service for signs of visible wear, may have contributed to the contamination of Soma 350 Tablets.

   Additionally, your firm failed to follow your procedures in documenting the frequency of cleaning the tooling used on the tablet presses.

The above items are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that the drug products you manufacture are in compliance with the Act and the regulations promulgated under it. Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the award of government contracts.

We have received your firm's written response, dated June 25, 2002, concerning our investigators' observations noted on the Form FDA 483 issued at the conclusion of the inspection on June 6, 2002. We recognize that your firm purchased the Soma 350 product line along with other products formerly manufactured by Carter-Wallace, Inc., in September 2001, and that your firm is presently in the process of [redacted] We also note that the presence of black specks can be traced back to 1983 and these issues were not fully investigated or resolved by the former firm. However, since July 2001, over [redacted] lots of Soma 350 Tablets have been manufactured, with the intent to increase inventory during your product [redacted] Studies conducted by consultants in October and November 2001, which were provided to our investigators on the last day of the inspection, attribute the presence of black specks to lubricant introduced from the upper cam into the empty die cavity. While your studies indicate these black specks are primarily lubricant spotting, trace amounts of metal were detected by your own studies. Study report PPD-02-5, submitted with your response, indicated metal abrasion occurring at the tooling keys, which could be a potential source for fine metal particles in the punch lubricant, however your investigations do not correlate this phenomenon to the tooling equipment taken out of service for excessive wear.

Your response included a health hazard assessment, dated June 20, 2002, conducted by an outside group; however we note this is a preliminary report. Your assessment that there is no identifiable health hazard associated with the spotting of Soma 350 Tablets cannot be considered conclusive until the final report is received and evaluated.

We disagree with your position that the presence of black specks is primarily an aesthetic issue. It is not acceptable to have visually observable contaminants in your finished dosage form products. It is the responsibility of your firm's Quality Unit to assure the identity, quality, strength and purity of your products and to assure that they meet all of their quality attributes. The quality standards established for Soma 350 Tablets, do not include visible specks on the tablet's surface.

Your response included numerous studies which were conducted -and corrective measures were suggested, such as the placements of seals to prevent the lubricant seeping and evaluating the condition of the tooling equipment. However there continues to be no approved final report with a plan to correct the problem prior to the [redacted].

Your response mentions that Lots 1G1054, 1H1061, 1I1083 and five other lots, which exhibited a higher rate of rejects after a second pass through the metal detector, have been placed on "hold" pending completion of your investigation. Please provide a copy of your rework/reprocessing procedure along with the results of your completed investigation and the disposition of these lots, with your further response.

You should take prompt action to correct deficiencies at your facility. Failure to implement corrective measures may result in further regulatory action without notice. These actions may include seizure of your products or injunction.

You should notify this office in writing within 15 working days or receipt of this letter of your corrective action plan to address the deficiencies at your firm. If corrective actions cannot be completed within 15 working days, please state the reason for the delay and the timeframe within which corrective actions will be completed. Your reply should be addressed to the Food and Drug Administration, New Jersey District Office, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054, Attn: Mercedes Mota, Compliance Officer.

Sincerely,

Douglas I. Ellsworth
District Director
New Jersey District

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